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Ambient Water Quality Criteria for Tetrachloroethylene

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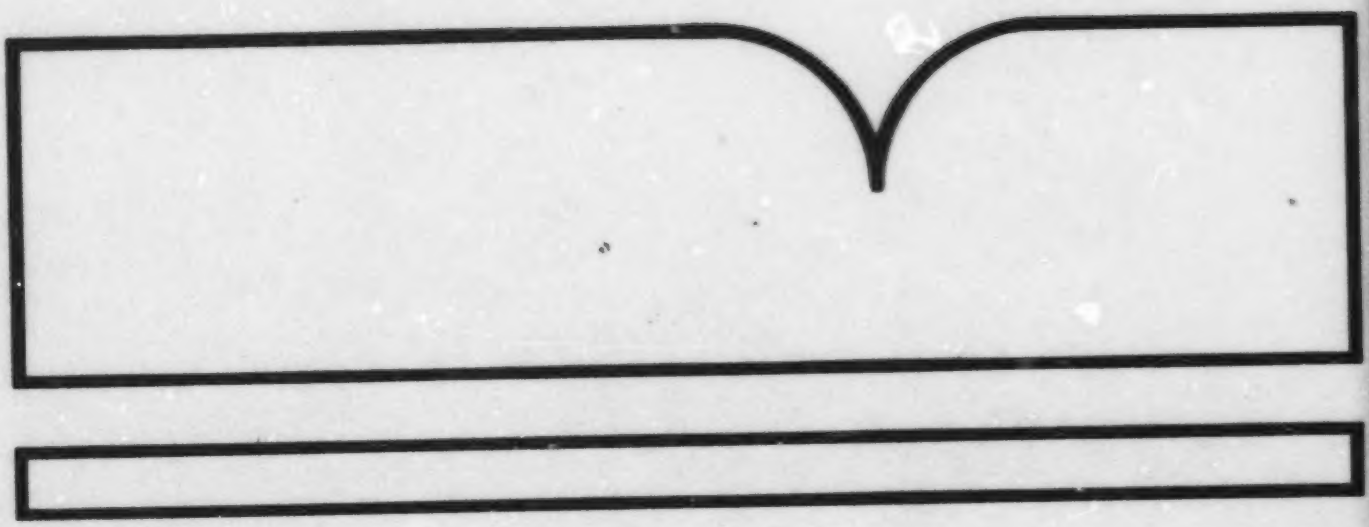

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Section 304(A) of the Clean Water Act [33 U.S.C. 1314(A)], requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for Tetrachloroethylene. It presents concentration criteria for the protection of freshwater and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A Section 304(A) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itself has no regulatory effect.

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AMBIENT WATER QUALITY CRITERIA FOR

TETRACHLOROETHYLENES

Prepared By
U.S. ENVIRONMENTAL PROTECTION AGENCY

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FOREWORD

Section 304 (a)(1) of the Clean Water Act of 1977 (P.L. 95-217), requires the Administrator of the Environmental Protection Agency to publish criteria for water quality accurately reflecting the latest scientific knowledge on the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of pollutants in any body of water, including ground water. Proposed water quality criteria for the 65 toxic pollutants listed under section 307 (a)(1) of the Clean Water Act were developed and a notice of their availability was published for public comment on March 15, 1979 (44 FR 15926), July 25, 1979 (44 FR 43660), and October 1, 1979 (44 FR 56628). This document is a revision of those proposed criteria based upon a consideration of comments received from other Federal Agencies, State agencies, special interest groups, and individual scientists. The criteria contained in this document replace any previously published EPA criteria for the 65 pollutants. This criterion document is also published in satisifaction of paragraph 11 of the Settlement Agreement in Natural Resources Defense Council, et. al. vs. Train, 8 ERC 2120 (D.D.C. 1976), modified, 12 ERC 1833 (D.D.C. 1979).

The term "water quality criteria" is used in two sections of the Clean Water Act, section 304 (a)(1) and section 303 (c)(2). The term has a different program impact in each section. In section 304, the term represents a non-regulatory, scientific assessment of ecological effects. The criteria presented in this publication are such scientific assessments. Such water quality criteria associated with specific stream uses when adopted as State water quality standards under section 303 become enforceable maximum acceptable levels of a pollutant in ambient waters. The water quality criteria adopted in the State water quality standards could have the same numerical limits as the criteria developed under section 304. However, in many situations States may want to adjust water quality criteria developed under section 304 to reflect local environmental conditions and human exposure patterns before incorporation into water quality standards. It is not until their adoption as part of the State water quality standards that the criteria become regulatory.

Guidelines to assist the States in the modification of criteria presented in this document, in the development of water quality standards, and in other water-related programs of this Agency, are being developed by EPA.

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Office of Water Regulations and Standards

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CRITERIA DOCUMENT

TETRACHLOROETHYLENE

CRITERIA

Aquatic Life

The available data for tetrachloroethylene indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 5,280 and 840 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for tetrachloroethylene indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 10,200 and 450 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Human Health

For the maximum protection of human health from the potential carcinogenic effects due to exposure of tetrachloroethylene through ingestion of contaminated water and contaminated aquatic organisms, the ambient water concentrations should be zero based on the non-threshold assumption for this chemical. However, zero level may not be attainable at the present time. Therefore, the levels which may result in incremental increase of cancer risk over the lifetime are estimated at 10^{-5}, 10^{-6}, and 10^{-7}. The corresponding recommended criteria are 8.0 µg/l, 0.80 µg/l, and 0.08 µg/l, respectively. If the above estimates are made for consumption of aquatic organisms only, excluding consumption of water, the levels are 88.5 µg/l, 8.85 µg/l, and 0.88 µg/l, respectively.

INTRODUCTION

Tetrachloroethylene (1,1,2,2-tetrachloroethylene, perchloroethlyene, PCE) is a colorless, nonflammable liquid used primarily as a solvent in the dry cleaning industries. It is used to a lesser extent as a degreasing solvent in metal industries (Windholz, 1976).

PCE has the molecular formula C_2Cl_4 and a molecular weight of 165.85. Other physical properties of PCE include a melting point of -23.25°C, a density of 1.623 g/ml, a vapor pressure of 19 mm Hg, a water solubility of 483 ug/ml and an octanol/water partition coefficient of 339 (log P = 2.53) (Patty, 1963; U.S. EPA, 1978a). The log P value indicates that PCE has an affinity for lipid material and may bioaccumulate.

Perchloroethylene can be widely distributed in the environment, as evidenced by its detection in trace amounts in U.S. and English waters, and in aquatic organisms, air, foodstuffs, and human tissue in England (McConnell, et al. 1975; U.S EPA, 1978b).

The highest levels of PCE are found in the work environments of the commercial dry cleaning and metal degreasing industries [National Institute for Occupational Safety and Health (NIOSH), 1976].

Although PCE is released into water via aqueous effluents from production plants, consumer industries, and household sewage, its level in ambient water is reported to be minimal due to its high volatility.

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Aquatic Life Toxicology*

INTRODUCTION

The data base for tetrachloroethylene and freshwater organisms indicates that the rainbow trout is most sensitive and the bluegill and fathead minnow are about as sensitive as Daphnia magna. An embryo-larval test has been conducted with the fathead minnow and the ratio between the acute and chronic values for this species is 16. The data for an alga indicate that it is much more resistant than the fishes and cladoceran. Compared to the dichloroethylenes and trichloroethylene, tetrachloroethylene is more acutely toxic to fish and invertebrate species.

Acute and chronic tests have been conducted with the mysid shrimp and the acute value is 23 times the chronic value which result suggests a substantial accumulative chronic toxicity. Compared to 1,1-dichloroethylene, tetrachloroethylene is much more toxic to the mysid shrimp. The saltwater alga, Skeletonema costatum, is much more resistant than the mysid shrimp, and the alga, Phaeodactylum tricornutum, has a resistance comparable to that for the mysid shrimp.

EFFECTS

Acute Toxicity

Daphnia magna has been tested with tetrachloroethylene (U.S. EPA, 1978) and the 48-hour EC_{50} is 17,700 ug/l (Table 1). The midge is only slightly more resistant with a 48-hour LC_{50} value of 30,840 ug/l.

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and Its Uses in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are calculations for deriving various measures of toxicity as described in the Guidelines.

The influence of the solvent carrier, dimethylformamide, has been studied using the rainbow trout (U.S. EPA, 1980), and the 96-hour LC_{50} values were 5,800 and 4,800 µg/l with and without the solvent, respectively (Table 1).

Alexander, et al. (1978) compared the toxicity of tetrachloroethylene to the fathead minnow using static unmeasured and flow-through measured procedures, the 96-hour LC_{50} values were 21,400 and 18,400 µg/l, respectively (Table 1). The flow-through result is consistent with that determined by U.S. EPA (1980) who reported a 96-hour LC_{50} of 13,460 µg/l. The bluegill (U.S. EPA, 1978) was similarly sensitive with a 96-hour LC_{50} value of 12,900 µg/l.

The data from acute static tests with the bluegill under similar conditions (U.S. EPA, 1978) in this and other documents on chloroethylenes show a correlation between increasing chlorination and toxicity. The 96-hour LC_{50} values for this species are 73,900 and 135,000 µg/l for 1,1- and 1,2-dichloroethylene, respectively, 44,700 µg/l for trichloroethylene, and 12,900 µg/l for tetrachloroethylene. These results indicate an increase in the lethal effect on bluegills with an increase in chlorination. This toxicity correlation for Daphnia magna data is not as clear. The 48-hour LC_{50} values were 79,000, 85,200, and 17,700 µg/l for 1,1-dichloroethylene, trichloroethylene, and tetrachloroethylene, respectively.

The mysid shrimp has been tested (U.S. EPA, 1978) using static unmeasured procedures, and the 96-hour LC_{50} value for sheepshead minnow was 10,200 µg/l (Table 1). The 96-hour LC_{50} value for sheepshead minnow is between 29,400 and 52,200 µg/l (Table 6).

The 96-hour LC_{50} for the mysid shrimp and tetrachloroethylene under static conditions is, as stated above, 10,200 µg/l (U.S. EPA, 1978). The

96-hour LC_{50} for the same species under similar test conditions (U.S. EPA, 1978) is 224,000 µg/l for 1,1-dichloroethylene. As was suggested in the freshwater part of this document, acute toxicity of these structurally related compounds increases with increasing chlorination.

Chronic Toxicity

A chronic value of 840 µg/l for the fathead minnow was obtained using embryo-larval test procedures (Table 2). This result together with the related LC_{50} value of 13,460 µg/l (Table 1) results in an acute-chronic ratio of 16.

The chronic value for the mysid shrimp was 450 µg/l (Table 2) and the acute-chronic ratio is 23. This ratio is very similar to that for the fathead minnow.

The geometric mean acute-chronic ratio for these two species is 19. A summary of species mean acute and chronic values is given in Table 3.

Plant Effects

No adverse effects on chlorophyll a or cell numbers of the freshwater alga, Selenastrum capricornutum, were observed at exposure concentrations as high as 816,000 µg/l (Table 4).

Two saltwater species have been tested, providing EC_{50} values that range from 10,500 to 509,000 µg/l (Table 4).

Residues

The bioconcentration factor for bluegill (U.S. EPA, 1978) was determined to be 49 using ^{14}C-tetrachloroethylene with verification by thin-layer chromatography (Table 5). Equilibrium was reached within 21 days and the depuration rate was rapid with a half-life of less than one day. Using similar methods (U.S. EPA, 1978), the bioconcentration factor for trichloroethylene was 17, not appreciably different from that for tetrachloroethylene. No comparable data are available for any dichloroethylene.

An estimated steady-state bioconcentration factor for tetrachloroethylene and the rainbow trout was determined by Neely, et al. (1974) to be 39 (Table 6).

Miscellaneous

Alexander, et al. (1978) also determined a 96-hour EC_{50} based on loss of equilibrium by the fathead minnow. This was 14,400 µg/l (Table 6), a concentration slightly lower than the 96-hour LC_{50} values of 18,400 and 21,400 µg/l for the same species.

As stated earlier, the 96-hour LC_{50} for the sheepshead minnow is between 29,400 and 52,200 µg/l (Table 6). No 96-hour LC_{50} could be calculated using the statistical procedures employed (U.S. EPA, 1978) since no data for partial mortality were obtained.

Summary

The acute toxicity results of tests with two freshwater invertebrate and three fish species and tetrachloroethylene range from 4,800 to 30,840 µg/l with no appreciable differences between or within those two groups. The chronic value for the fathead minnow is 840 µg/l, which result provides an acute-chronic ratio of 16. The freshwater alga, Selenastrum capricornutum, was much more resistant than the invertebrate and fish species with no observed effects at concentrations as high as 816,000 µg/l. Estimated and measured bioconcentration factors for two fish species were within the range of 39 to 49.

For mysid shrimp the 96-hour LC_{50} and chronic values for tetrachloroethylene were 10,200 and 450 µg/l, respectively, and these results yield an acute-chronic ratio of 23. The saltwater alga, Skeletonema costatum, was much more resistant than the shrimp with observed effects in the range of 504,000 to 509,000 µg/l. Another algal species, Phaeodactylum tricornutum, was more sensitive with an EC_{50} of 10,500 µg/l.

CRITERIA

The available data for tetrachloroethylene indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 5,280 and 840 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for tetrachloroethylene indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 10,200 and 450 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Table 1. Acute values for tetrachloroethylene

Species	Method[a]	LC50/EC50 (µg/l)	Species Acute Value (µg/l)	Reference
		FRESHWATER SPECIES		
Cladoceran, Daphnia magna	S, U	17,700	17,700	U.S. EPA, 1978
Midge, Tanytarsus dissimilis	S, M	30,840	30,840	U.S. EPA, 1980
Rainbow trout, Salmo gairdneri	FT, M	4,800	-	U.S. EPA, 1980
Rainbow trout, Salmo gairdneri	FT, M	5,800	5,280	U.S. EPA, 1980
Fathead minnow, Pimephales promelas	FT, M	13,460	-	U.S. EPA, 1980
Fathead minnow, Pimephales promelas	FT, M	18,400	-	Alexander, et al. 1978
Fathead minnow, Pimephales promelas	S, U	21,400	15,700	Alexander, et al. 1978
Bluegill, Lepomis macrochirus	S, U	12,900	12,900	U.S. EPA, 1978
		SALTWATER SPECIES		
Mysid shrimp, Mysidopsis bahia	S, U	10,200	10,200	U.S. EPA, 1978

[a] S = static, FT = flow-through, U = unmeasured, M = measured

No Final Acute Values are calculable since the minimum data base requirements are not met.

Table 2. Chronic values for tetrachloroethylene

Species	Method*	Limits (µg/l)	Chronic Value (µg/l)	Reference
		FRESHWATER SPECIES		
Fathead minnow, *Pimephales promelas*	E-L	500-1,400	840	U.S. EPA, 1980
		SALTWATER SPECIES		
Mysid shrimp, *Mysidopsis bahia*	LC	300-670	450	U.S. EPA, 1978

* E-L = embryo-larval, LC = life cycle or partial life cycle

Acute-Chronic Ratio

Species	Chronic Value (µg/l)	Acute Value (µg/l)	Ratio
Fathead minnow, *Pimephales promelas*	840	13,460*	16
Mysid shrimp, *Mysidopsis bahia*	450	10,200	23

*This acute value was selected because it was determined by the same investigator who determined the chronic value.

Geometric mean acute-chronic ratio = 19

Table 3. Species mean acute and chronic values for tetrachloroethylene

Number	Species	Species Mean Acute Value* (µg/l)	Species Mean Chronic Value (µg/l)	Acute-Chronic Ratio**
		FRESHWATER SPECIES		
5	Midge, *Tanytarsus dissimilis*	30,840	-	-
4	Cladoceran, *Daphnia magna*	17,700	-	-
3	Fathead minnow, *Pimephales promelas*	15,700	840	16
2	Bluegill, *Lepomis macrochirus*	12,900	-	-
1	Rainbow trout, *Salmo gairdneri*	5,280	-	-
		SALTWATER SPECIES		
1	Mysid shrimp, *Mysidopsis bahia*	10,200	450	23

* Rank from high concentration to low concentration by species mean acute value.

**See the Guidelines for derivation of this ratio.

Table 4. Plant values for tetrachloroethylene

Species	Effect	Result (µg/l)	Reference
	FRESHWATER SPECIES		
Alga, *Selenastrum capricornutum*	Chlorophyll *a* 96-hr EC50	>816,000	U.S. EPA, 1978
Alga, *Selenastrum capricornutum*	Cell number 96-hr EC50	>816,000	U.S. EPA, 1978
	SALTWATER SPECIES		
Alga, *Phaeodactylum tricornutum*	EC50	10,500	Pearson & McConnell, 1975
Alga, *Skeletonema costatum*	Chlorophyll *a* 96-hr EC50	509,000	U.S. EPA, 1978
Alga, *Skeletonema costatum*	Cell number 96-hr EC50	504,000	U.S. EPA, 1978

Table 5. Residues for tetrachloroethylene (U.S. EPA, 1978)

Species	Tissue	Bioconcentration Factor	Duration (days)
	FRESHWATER SPECIES		
Bluegill, *Lepomis macrochirus*	whole body	49	21

Table 6. Other data for tetrachloroethylene

Species	Duration	Effect	Result (µg/l)	Reference
		FRESHWATER SPECIES		
Rainbow trout, *Salmo gairdneri*	-	Estimated steady-state bioconcentration factor = 39	-	Neely, et al. 1974
Fathead minnow, *Pimephales promelas*	96 hrs	Loss of equilibrium, EC50	14,400	Alexander, et al. 1978
		SALTWATER SPECIES		
Sheepshead minnow, *Cyprinodon variegatus*	96 hrs	LC50	>29,400 <52,200	U.S. EPA, 1978

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Mammalian Toxicology and Human Health Effects

EXPOSURE

Ingestion from Water

The National Organics Monitoring Survey (U.S. EPA, 1978a) detected tetrachloroethylene (perchloroethylene, PCE) in nine of 105 drinking waters sampled between November 1976 and January 1977 (range, < 0.2 to 3.1 µg/l; median < 0.2 µg/l). The mean concentration of the nine positive samples was 0.81 µg/l. In Switzerland, PCE concentrations have been found in contaminated ground water as high as 954 µg/l (Giger and Molner-Kubiea, 1978). PCE was one of two halogenated compounds identified both in the drinking water and in the plasma of individuals living in New Orleans (Dowty, et al. 1975). In the British Isles, municipal waters have been found to contain up to 0.38 µg PCE/l (Pearson and McConnell, 1975). It is presently possible to detect 10 ppt tetrachlorethylene in water by electron capture and liquid-liquid extraction techniques.

Ingestion from Food

PCE concentrations in seafood collected from the Liverpool Bay (England) area ranged from 0.5 to 30 µg/kg (Pearson and McConnell, 1975; Dickson and Riley, 1976). Corresponding concentrations in the seawater were, mean 0.12 µg/l, maximum 2.6 µg/l (Pearson and McConnell, 1975). PCE concentrations in foods ranged from non-detectable amounts (<0.01 µg/kg) in orange juice to 13 µg/kg in English butter (McConnell, et al. 1975). These data, however, apply to the British Isles. No such data appear to exist for the United States.

A bioconcentration factor (BCF) relates the concentration of a chemical in aquatic animals to the concentration in the water in which they live. The steady-state BCFs for a lipid-soluble compound in the tissues of various aquatic animals seem to be proportional to the percent lipid in the tissue. Thus, the per capita ingestion of a lipid-soluble chemical can be estimated from the per capita consumption of fish and shellfish, the weighted average percent lipids of consumed fish and shellfish, and a steady-state BCF for the chemical.

Data from a recent survey on fish and shellfish consumption in the United States were analyzed by SRI International (U.S. EPA, 1980). These data were used to estimate that the per capita consumption of freshwater and estuarine fish and shellfish in the United States is 6.5 g/day (Stephan, 1980). In addition, these data were used with data on the fat content of the edible portion of the same species to estimate that the weighted average percent lipids for consumed freshwater and estuarine fish and shellfish is 3.0 percent.

A measured steady-state bioconcentration factor of 49 was obtained for tetrachloroethylene using bluegills (U.S. EPA, 1978b). Similar bluegills contained an average of 4.8 percent lipids (Johnson, 1980). An adjustment factor of 3.0/4.8 = 0.625 can be used to adjust the measured BCF from the 4.8 percent lipids of the bluegill to the 3.0 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factor for tetrachloroethylene and the edible portion of all freshwater and estuarine aquatic organisms consumed by Americans is calculated to be 49 x 0.625 = 30.6.

Inhalation

General environmental PCE concentrations tend to be low. Pearson and McConnell (1975) observed concentrations in city atmospheres in Great Britain ranging from less than 0.68 to 68 $\mu g/m^3$. In a suburb of Munich, Loechner (1976) found concentrations of 4 μg PCE/m^3 whereas air in the center of Munich contained 6 $\mu g/m^3$. Surveys at eight locations in the U.S. indicated concentrations up to 6.7 $\mu g/m^3$ as observed in urban areas and less than 0.013 $\mu g/m^3$ in rural areas (Lillian, et al. 1975). As with a number of related, low molecular weight, chlorinated hydrocarbon solvents by far the most significant exposure to PCE is in industrial environments (Fishbein, 1976). The major uses of PCE are in textile and dry cleaning industries (69 percent), metal cleaning (16 percent), and as a chemical intermediate (12 percent). Exposure to as much as 178 ppm (eight-hour, time-weighted average) of PCE have been observed in the dry cleaning industry, particularly during high production periods [National Institute for Occupational Safety and Health (NIOSH), 1974].

Dermal

As with inhalation exposures, dermal exposures of significance would be primarily confined to occupational exposure.

PHARMACOKINETICS

Absorption

Using inhalation exposure, Stewart, et al. (1961a) found that PCE reached near steady-state levels in blood of human volunteers with two hours of continuous exposure. Such results suggest a rapid attainment of steady-state levels of PCE within the body.

This may be deceptive, however, since the biological half-life of PCE metabolites (as measured as total trichloro compounds) is 144 hours (Ikeda and Imamura, 1973). The relative stability of PCE concentrations in blood beyond two hours probably represents a redistribution phenomenon common to a number of volatile anesthetics (Goodman and Gilman, 1966). Later studies (Stewart, et al. 1970) have shown that PCE concentrations in expired air immediately following exposure increase with repeated exposures over a five day period. These data confirm that the steady-state implied by the leveling off of blood PCE concentrations has not been reached with short-term exposures. Retention of inhaled PCE has been estimated to approximate 57 percent of the administered dose (Ogata, et al. 1971).

Stewart and Dodd (1964) demonstrated absorption of PCE through the skin by immersing the thumbs of volunteers in PCE for 40 minutes and measuring the PCE in the exhaled air. High concentrations of PCE in exhaled breath (160 to 260 $\mu g/m^3$) were measurable five hours after exposure.

Distribution

Once in the body, PCE tends to distribute to body fat. Although the human data available are quite limited, in those individuals which have significant body burdens (subjects E and F in Table 1), ratios of fat to liver concentrations are greater than six.

A more marked distribution of PCE to fat is observed using controlled exposures to rats. The data in Table 2 (Savolainen, et al. 1977) were obtained from animals who had been exposed to 1,340

TABLE 1

Distribution of Tetrachloroethylene
in Human Tissue at Autopsy*

Concentrations in µg/kg (wet tissue)				
Subject	Age	Sex	Tissue	Tetrachloro-ethylene
A	76	F	Body fat	6
			Kidney	0.5
			Liver	0.5
			Brain	0.5
B	76	F	Body fat	1
			Kidney	6
			Liver	2
			Brain	5
C	82	F	Body fat	0.4
			Liver	1.2
D	48	M	Body fat	0.8
			Liver	0.7
E	65	M	Body fat	21
			Liver	3.4
F	75	M	Body fat	29.2
			Liver	4.3
G	66	M	Body fat	0.5
H	74	F	Body fat	4

*Source: McConnell, et al. 1975

TABLE 2

Changes in the Organ Content of PCE with Duration of Exposure in Rats Having Prior History of PCE Exposure[a]

Duration of Exposure (h)	Concentration[b]					
	Cerebrum	Cerebellum	Lungs	Liver	Perirenal Fat	Blood
0	3.1 + 0.6	2.2 + 0.7	1.6 + 0.3	5.8 + 1.5	103 + 3	0.7 + 0.2
2	14.9 + 2.8	10.3 + 1.2	7.6 + 1.7	17.8 + 4.5	162 + 29	3.5 + 0.7
3	18.0 + 0.8	12.0 + 0.7	8.7 + 1.6	22.4 + 0.2	134 + 6	4.2 + 0.2
4	16.8 + 2.9	11.3 + 0.9	9.9 + 2.2	22.2 + 0.1	183 + 32	4.1 + 0.6
6	23.7 + 1.2	15.3 + 0.2	12.2 + 0.6	26.7 + 4.0	286 + 70	5.0 + 1.1

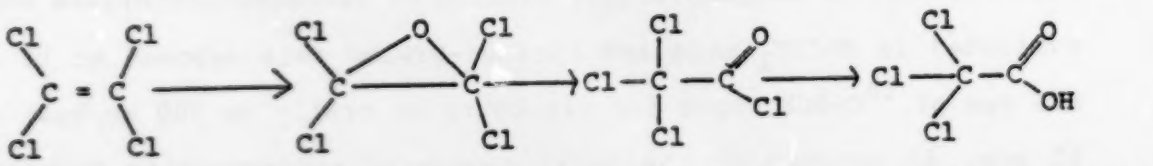
[a]Source: Savolainen, et al. 1977

[b]µg/g wet weight of tissue or µg/ml blood + range of two animals

mg/m^3 of PCE for six hours/day on four prior days. The zero time values represent the residual PCE from these previous exposures on the fifth day. Each succeeding time interval indicates the kinetics of PCE build-up in each organ with the identical exposure conditions on day 5. As can be seen in the table, a substantial residual concentration of PCE is found in fat from the previous exposures. PCE levels rise more or less continuously with duration of exposure in brain, lungs, and fat, but tend to level out in blood and liver after a three hour exposure. It is notable that brain concentrations of PCE exceed blood levels by about fourfold and are independent of duration of the exposure. On the other hand, the ratio of concentration in fat relative to blood decreases approximately 150:1 to 50:1 over the course of the exposure. These data suggest that turnover of PCE in fat is slower than that observed in other tissues.

Metabolism

Metabolism of PCE has been studied extensively in humans and experimental animals. In a qualitative sense metabolic products appear to be similar in humans (Ikeda, et al. 1972; Ikeda, 1977) and experimental animals (Yllner, 1961; Daniel, 1963; Ikeda and Ohtsuji, 1972). The metabolic pathway is summarized:



A similar reaction has been observed when PCE is exposed to oxygen, excess chlorine, and sunlight at 36 to 40°C (Frankel, et al. 1957). It has been postulated that the symmetrical epoxide formed from tetrachloroethylene is not mutagenic (in E. coli K_{12}) because it is more stable and less reactive towards cellular nucleophiles than the unsymmetrical epoxides formed from vinyl chloride, 1,1-dichloroethylene, and trichloroethylene, (Henschler, et al. 1976; Henschler, 1977b).

Ogata, et al (1971) reported that 1.8 percent of PCE retained by humans was converted to trichloroacetic acid and 1.0 percent to an unknown metabolite in 67 hours. Metabolism of PCE is apparently saturable, in that exposures exceeding 70 mg/m^3 do not increase excretion of trichloroacetic acid in the urine (Ikeda, 1977). However, metabolism of PCE is inducible by phenobarbital (Ikeda and Imamura, 1973) and Aroclor 1254* (Moslen, et al. 1977), suggesting that a higher percentage of metabolic conversion is possible under certain conditions.

Schumann, et al. (1979) recently showed that the $B6C3F_1$ mouse metabolizes a significantly greater proportion of doses of PCE than does the Sprague-Dawley rat, and that the reactive metabolites of PCE are bound to hepatic macromolecules in the mouse to a greater degree than in the rat. Species differences regarding the metabolism and hepatic macromolecular binding of tetrachloroethylene were evaluated in $B6C3F_1$ mice and Sprague-Dawley rats exposed to 10 or 600 ppm of ^{14}C-PCE vapor for six hours or orally to 500 mg/kg. At 10 ppm, 63 percent of the total recovered radioactivity from the mouse appeared in the urine as nonvolatile metabolite(s) and 12

*Registered Tradename for a mixture of polychlorinated biphenyls

percent was excreted unchanged in expired air (19 and 68 percent, respectively, for the rat). The mouse metabolized 7 to 8 times more PCE per kg of body weight than did the rat following 10 ppm and 1.6 times at 500 mg/kg. Approximately 7 to 9 times more radioactivity was irreversibly bound to hepatic macromolecules in the mouse than in the rat at all exposure levels. No radioactivity was detected bound to purified hepatic DNA at times of peak macromolecular binding in the mouse. These results support the view that mice are more sensitive than rats to the hepatic effects of PCE due to greater metabolism of PCE to a reactive intermediate(s).

Excretion

PCE itself is primarily eliminated in humans from the body via the lungs. The respiratory half-time for PCE elimination has been estimated at 65 hours (Stewart, et al. 1961a, 1970; Ikeda and Imamura, 1973).

Trichloroacetic acid, as a metabolite of PCE, is eliminated, with a half-time of 144 hours, via the urine (Ikeda and Imamura, 1973). Since the half-time for elimination of trichloroacetic acid as a metabolite of trichloroethylene is only 36 to 58 hours in normal humans (Ikeda and Imamura, 1973), this rate is more a reflection of delayed respiratory turnover of the parent compound than for trichloroacetic acid itself. In all likelihood this is a result of the greater lipophilicity of PCE relative to trichloroethylene.

EFFECTS

Acute, Subacute, and Chronic Toxicity

As with all other members of the chloroethylene family, acute effects of PCE are very much dominated by central nervous system depression. Because of its widespread use in industry the acute effects on the central nervous system of PCE have been studied under controlled conditions using human volunteers. The first of these studies, by Carpenter (1937), exposed individuals to concentrations of PCE averaging 3,183 and 6,258 mg/m^3 for 95 and 130 minutes, respectively. At the low concentration sensory changes and a slight feeling of elation were observed. However, at the higher concentration more definite signs of central nervous system depression were observed, i.e., lassitude, mental fogginess and exhilaration. When this concentration was raised to 10,000 mg/m^3 signs of inebriation were observed and at 13,400 mg/m^3 all were forced to leave the chamber within 7.5 minutes. Rowe, et al. (1952) reported the exposure of humans to vapor concentrations of PCE averaging 710 mg/m^3 failed to produce significant central nervous system effects whereas minimal effects could be observed at 1,340 mg/m^3.

Stewart, et al. (1961a) noted impaired ability to perform a Romberg test, a measure of reflex coordination, in volunteers subjected to 1,300 mg/m^3 for more than 30 minutes. In a later paper this same group (Stewart, et al. 1970), found that three of their subjects were not capable of performing a normal Romberg test after three hours of exposure to 670 mg/m^3 PCE. In addition, 25 percent of the individuals reported subjective complaints ranging from mild irritation, lightheadedness and mild frontal headache, to feeling slightly sleepy and experiencing some difficulty in speaking.

More recently, Stewart, et al. (1977) examined a group of 12 volunteers exposed to 168 and 670 mg PCE/m^3 for 5.5 hours a day repeated up to 53 days. In this study they were unable to document any consistent neurological changes due to PCE exposure, although they did observe a statistically significant decrement in the performance of a Flanagan coordination test (which the authors stated as being inconsistent). In a group of workers occupationally exposed to concentrations of approximately 400 mg/m^3 (one for 15 years) subjective complaints, such as headache, fatigue, somnolence, dizziness, and a sensation of intoxication were noted (Medek and Kovarik, 1973). In confirmation of shorter-term volunteer studies no objective neurological effects could be associated with PCE exposure.

Rowe, et al. (1952) indicated that rats, guinea pigs, rabbits and monkeys exposed repeatedly for seven hours per day displayed no changes in behavior at vapor concentrations of PCE up to 2,720 mg/m^3. At 10,999 mg/m^3, rats were drowsy during the first week of exposure. However, in the second week marked salivation, restlessness, irritability, and loss of equilibrium and coordination were observed. Rowe, et al. (1952) suggested that this resulted from an hypercholinergic state since the excited state could be prevented by atropine.

Goldberg, et al. (1964) reported that PCE caused an 80 percent loss of both avoidance and escape responses in rats after a single four-hour exposure to 15,400 mg/m^3. These effects were primarily attributable to an overt ataxia. In contrast, Savolainen, et al. (1977) observed increased ambulation in the open field by rats

exposed to 1,340 mg/m^3 for five days, six hours daily. These changes were paralleled by a small but significant decrease in brain RNA content and an increase in nonspecific cholinesterase activity. The only indications of long-term effects on the central nervous system are findings of changed EEG patterns in rats associated with increased electrical impedence of the cerebral cortex at exposures as low as 100 mg PCE/m^3, 4 hour/day for 15 to 30 days (Dmitrieva, 1966; Dmitrieva and Kuleshov, 1971). These effects were reported to be associated with sporadic swollen and vacuolized protoplasm in some cells (Dmitrieva and Kuleshov, 1971). Although information available from experimental animals is limited, it generally supports findings of acute central nervous system depression. As in the case of human clinical studies essentially no information is available concerning long term effects (i.e., greater than one week exposures) of PCE on the central nervous system. As suggested by Stewart, et al. (1970), the current threshold limit value (50 ppm) [American Conference of Governmental Industrial Hygienists (ACGIH), 1977] for PCE has a negligible factor of safety even for short-term exposures. That more serious central nervous system problems may be associated with chronic PCE exposure is suggested by a few sporadic case reports (Gold, 1969; McMullen, 1976) and small scale epidemiological and clinical studies (Coler and Rossmiller, 1953). However, the latter studies have often been complicated by exposures to other solvents (Tuttle, et al. 1977).

Short-term PCE exposures at higher concentrations can produce damage to kidney and liver (Klaasen and Plaa, 1967). Increased weight and mild to marked central fatty degeneration of the liver

were observed with up to 158 repeated 7-hour exposures of guinea pigs to PCE at 670 to 16,750 mg/m^3 (Rowe, et al. 1952). Lower concentrations appeared to be less effective. Rabbits, rats, and monkeys appeared less sensitive in that no significant effects were observed following repeated 7-hour exposures at concentrations up to 2,680 mg/m^3. Rowe, et al. (1952) indicated that at 2,680 mg PCE/m^3 increased kidney weights were also observed in guinea pigs but not in other species. However, the prior work of Carpenter (1937) had shown congestion and granular swelling in the kidney of rats exposed for eight hours, five days per week over a period of seven months to 1,540 mg/m^3. More recently, the National Cancer Institute's (NCI) carcinogenesis bioassay of PCE revealed a high incidence of toxic nephropathy in both male and female $B6C3F_1$ mice exposed orally to 536 and 386 mg PCE/kg, respectively, for five days a week for 78 weeks (NCI, 1977). Similar results were obtained in both male and female Osborne-Mendel rats exposed to 471 and 474 mg PCE/kg, respectively, over the same treatment course.

Kylin, et al. (1963) noted moderate fatty degeneration of the liver with a single 240 minute exposure to 1,340 mg PCE/m^3. Exposure to this same concentration four hours daily, six days a week for up to eight weeks was found to increase the severity of the lesions caused by PCE (Kylin, et al. 1965).

Fujii (1975) dosed male rabbits once orally with 2,158 mg/kg of PCE and observed increases in serum lipoprotein concentrations which were still evident two weeks after treatment. Changes in serum enzyme activities (i.e., alkaline phosphatase, glutamate-oxalacetate transaminase, glutamate-pyruvate transaminase), indic-

ative of liver damage, were mild and transient. Single doses of PCE (0.3 to 2.0 ml/kg) injected by Cornish, et al. (1973), appeared to increase serum glutamate oxalacetate transaminase activity.

Liver and/or kidney damage in humans have been reported. Out of six case histories of acute, high-level inhalation exposure to PCE where there was evidence of liver damage (Hughes, 1954; Stewart, et al. 1961b; Meckler and Phelps, 1966; Saland, 1967; Stewart, 1969; Hake and Stewart, 1977), kidney damage was detected in just one individual (Hake and Stewart, 1977). Hepatic injury itself is uncommon in persons exposed to PCE vapors, as there are numerous accounts of intoxication where there was no detectable organ damage.

The data of Coler and Rossmiller (1953) involving a group of men occupationally exposed to concentrations of 1,890 to 2,600 mg/m^3 of PCE supports animal data indicating that liver injury may result from PCE. Three of seven men had evidence of impaired liver function. An individual accidentally acutely exposed to an anesthetic dose of PCE exhibited a transient increase in serum glutamate oxalacetate transaminase activity and a delayed elevation of urinary urobilinogen, both indicative of hepatic injury (Stewart, 1969).

The possible cardiovascular effects of PCE have not been systematically investigated. Unlike its analog, trichloroethylene, PCE does not appear to sensitize the myocardium to epinephrine (Reinhardt, et al. 1973). However, in controlled human studies involving exposure to PCE at 1,140 mg/m^3 for three hours Ogata, et

al. (1971) indicated an increase of diastolic blood pressure averaging 15 mm Hg compared to a decrease of 5 mm Hg in a non-exposed group over the same time interval. Systolic blood pressure changed only slightly in both groups (+2 mm Hg with PCE and -4 mm Hg in controls). Although not specifically addressed in the discussion of the results, a group of six volunteers exposed to 1,300 mg PCE/m^3 for 187 minutes uniformly showed an increase in systolic blood pressure which averaged 13 mm Hg (Stewart, et al. 1961a). Other groups exposed to the same concentration for only 83 minutes or to a lower concentration of PCE (670 mg/m^3), showed no consistent change in blood pressure.

PCE, as with a number of other low molecular weight chlorinated compounds, greatly increases bile duct-pancreatic fluid flow in rats (Hamada and Peterson, 1977). The resulting fluid has a markedly depressed protein content and a significantly altered ionic composition. The physiological significance of these observations has not yet been determined.

Occasional reports have associated PCE with the symptomatology of more serious chronic diseases such as Raynaud's disease (Lob, 1957; Sparrow, 1977). Sparrow (1977) has reported a case which involved depressed immune function, mildly depressed liver function, polymyopathy, and severe acrocyanosis. Such isolated reports are difficult to evaluate, but deserve mention here because of a similar disease which has been observed in vinyl chloride workers. It should be noted here that very little work has been done to delineate the absorption and distribution of orally ingested PCE.

Synergism and/or Antagonism

As PCE is metabolized by mixed function oxidases, compounds which alter the functional activity of this system might be expected to affect its toxicity. Cornish, et al. (1973, 1977), however, were unable to demonstrate that phenobarbital pretreatment was capable of modifying the hepatotoxicity of PCE. Moslen, et al. (1977) and Reynolds and Moslen (1977) report that PCE produces vacuolization of rough endoplasmic reticulum and increases in serum glutamate oxalacetate transaminase activity following Aroclor 1254® induction of mixed function oxidases. It must be kept in mind that only a small percent of retained PCE is metabolized when compared to other members of the chloroethylene series (Ogata, et al. 1971). Consequently, both the experiments conducted by Moslen, et al. (1977) and Reynolds and Moslen (1977) were of too short duration to fully assess the influence of metabolism on the long-term toxicity of PCE.

Intolerance of alcohol has been reported with PCE exposure (Gold, 1969). As both compounds are central nervous system depressants such effects are to be expected. There do not appear to be any documented metabolic interactions of PCE with alcohol as there are with trichloroethylene (Cornish and Adefuin, 1966; Gessner, 1973). Stewart, et al. (1977) were unable to document any significant interactions between alcohol or diazepam with PCE exposures up to 670 mg/m^3. However, the question of synergism between ethanol and PCE has not been addressed experimentally over a sufficiently large dose range to rule out such an interaction.

PCE interactions with benzene and toluene have been studied systematically with lethality as an endpoint (Withey and Hall, 1975). Intubation of rats with mixtures of benzene and PCE yielded a combined toxicity which was only slightly less than additive. Mixtures of toluene and PCE resulted in LD_{50} values of less than that predicted for simple additivity, indicating synergistic effects.

Since PCE is metabolized to trichloroacetic acid there may be a possibility of its synergizing with compounds, such as warfarin, that bind significantly with serum albumin (Wardell, 1974). Although this has been suggested for trichloroethylene (Ertle, et al. 1972), this question has not been systematically investigated with PCE.

Teratogenicity

Only one report has appeared concerning the possibility of PCE-induced teratogenesis (Schwetz, et al. 1975). Female rats and mice were exposed to 2,000 mg PCE/m^3 for seven hours daily on days 6 to 15 of gestation. Primary effects of PCE included a decrease in fetal body weight of mice, a small but significant increase in fetal resorptions in the rat, subcutaneous edema in mice pups, and delayed ossification of skull bones and sternabrae in the mice. These effects were mild, leading the authors to conclude that PCE was not teratogenic. However, it must be pointed out that these experiments were conducted with only one dose, which was only three times greater than the current TLV and involved intermittent (i.e., seven hours/day) exposure to the chemical during a limited segment (10 days) of a short gestational period (21 days). If PCE behaves

in mice as it does in humans, at least five days exposure would be necessary to achieve steady-state concentrations in the animal. Although the effects were minor, they were statistically significant. Additional work is necessary to clarify whether PCE possesses teratogenic activity.

Mutagenicity

Henschler (1977a,b) and coworkers have postulated that the mutagenicity and carcinogenicity of chloroethylenes are dependent upon the reactivity of their metabolically formed epoxide intermediates. Unsymmetrically substituted chlorines result in unbalanced electron withdrawal by chlorine atoms and a more reactive epoxide intermediate. Support for this hypothesis is gained from the demonstration of an increased rate of spontaneous mutation in E. coli K_{12} in the presence of liver microsomes when treated with chloroethylene (vinyl chloride), 1,1-dichloroethylene, and trichloroethylene, and an absence of increased rate of mutation with the symmetrically substituted 1,2-dichloroethylenes and tetrachloroethylene (Greim, et al. 1975). Comparison of the compounds using Salmonella typhimurium was said not to be possible because of a high primary toxicity of some of the compounds (Henschler, 1977a,b). Nevertheless, Cerna and Kypenova (1977) indicate finding elevated mutagenic activity in Salmonella strains sensitive to both base substitution and frameshift mutation treated with PCE and cis-1,2-dichloroethylene, both symmetrically substituted compounds. However, these data are insufficient evidence as to the mutagenicity of PCE.

Bonse, et al. (1975) has shown that tetrachloroethylene oxide was reasonably stable but that the trichloroacetyl chloride formed from the epoxide was highly reactive. The acyl halide was found to covalently bind with cellular constituents. This may account for the discrepancy of the prediction of Henschler (1977b) regarding the carcinogenicity of PCE (NCI, 1977).

Carcinogenicity

PCE has been demonstrated to be a liver carcinogen in $B6C3F_1$ mice (NCI, 1977). Results in Osborne-Mendel rats were negative, but a high rate of early mortality precluded use of rat data in evaluating the carcinogenicity of PCE. Furthermore, recent data in which carbon tetrachloride was used as a positive control revealed that Osborne-Mendel rats have a low sensitivity to induction of hepatocellular carcinoma by chlorinated organic compounds in general (NCI, 1976).

The only tumor which occurred in either male or female $B6C3F_1$ mice that could be related to PCE administration was hepatocellular carcinoma. The data are depicted in Table 3.

Low dose males received a time weighted average dose of 536 mg/kg, 5 days/week for 78 weeks. High dose males received 1,072 mg/kg on the same schedule. Low dose and high dose female groups received 386 and 772 mg/kg, respectively, also on the same schedule.

Male and female rats exposed for 12 months to 300 and 600 ppm of a PCE formulation by inhalation did not show evidence of carcinogenic effects during the 12-month observation period following termination of exposure (Leong, et al. 1975). However, the mortal-

TABLE 3

Incidence of Hepatocellular Carcinoma
in PCE-treated $B6C3F_1$ Mice*

	Males		Females	
Control	2/17		2/20	
Vehicle Control	2/20		0/20	
Low dose	32/49	(536 mg/kg)	19/48	(386 mg/kg)
High dose	27/48	(1,072 mg/kg)	19/49	(772 mg/kg)

*Source: NCI, 1977

ity of male rats exposed to 600 ppm was significantly higher than that of the controls. Gross pathological examination failed to detect any differences between either treatment group and the controls.

No systematic studies of PCE exposure and the incidence of human cancer seem to be available.

CRITERION FORMULATION

Existing Guidelines and Standards

Existing tetrachloroethylene (PCE) standards are primarily applicable to occupational exposures. The American Conference of Governmental Industrial Hygienists threshold limit value (TLV), listed in Table 4, has been established primarily on the basis of measurable deficits in central nervous system function resulting from short-term exposures of healthy male volunteers. As Stewart, et al. (1970) point out, this figure incorporates a negligible factor of safety even for this group. Thus, sensitive populations or the possibility of other environmental conditions which might synergize with PCE toxicity have not been considered (ACGIH, 1977). Additionally, it does not yet incorporate consideration of PCE carcinogenicity (NCI, 1977).

Current Levels of Exposure

The National Organics Monitoring Survey (U.S. EPA, 1978a) detected tetrachloroethylene (perchloroethylene, PCE) in nine of 105 drinking waters sampled between November 1976 and January 1977 (range, < 0.2 to 3.1 µg/l; median < 0.2 µg/l). The mean concentration of the nine positive samples was 0.81 µg/l. PCE was one of two halogenated compounds indentified both in the drinking water and in the plasma of individuals living in New Orleans (Dowty, et al. 1975).

No data were found on levels of PCE in United States food. In England, PCE concentrations in foods ranged from nondetectable amounts (< 0.01 µg/kg) in orange juice to 13 µg/kg in English butter (McConnell, et al. 1975).

TABLE 4

Industrial Hygiene Standards for
Tetrachloroethylene in Various Countries*

	mg/m^3	Calculated Allowable Daily Exposure mg/day
USA	670	4,793
German Democratic Republic	250	1,786
USSR	1	7

*Source: Fishbein, 1976

General environmental PCE concentrations tend to be low. Surveys at eight locations in the U.S. found concentrations of up to 6.7 $\mu g/m^3$ in urban areas and less than 0.013 $\mu g/m^3$ in rural areas (Lillian, et al. 1975). By far the most significant exposure to PCE occurs in industrial environments (Fishbein, 1976). The major uses of PCE are in textile and dry cleaning industries (69 percent), metal cleaning (16 percent), and as a chemical intermediate (12 percent). As with inhalation exposures, dermal exposures of significance would be primarily confined to occupational exposure.

Basis and Derivation of Criterion

No additional human or animal data exist that may be used to refine the AGCIH estimate of noncarcinogenic risks from exposure to PCE, with the exception of the data of Dmitrieva (1966) and Dmitrieva and Kuleshov (1971). These Russian papers suggest that central nervous system effects can be observed in rats at exposures to PCE as low as 100 mg/m^3 in an experiment lasting five months.

Under the Consent Decree in NRDC v. Train, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Tetrachloroethylene is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of tetrachloroethylene in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and states in the possible future development of water quality regulations, the con-

centrations of tetrachloroethylene corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the Federal Register notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6}, or 10^{-7} as shown in the following table.

Exposure Assumptions (per day)	Risk Levels and Corresponding Criteria(1)		
	10^{-7}	10^{-6}	10^{-5}
2 l of drinking water and consumption of 6.5 g fish and shellfish. (2)	0.08 µg/l	0.80 µg/l	8.00 µg/l
Consumption of fish and shellfish only.	0.88 µg/l	8.85 µg/l	88.5 µg/l

(1) Calculated by applying a linearized multistage model as discussed in the Human Health Methodology Appendices to the October 1980 Federal Register notice which announced the availability of this document, to the animal bioassay data presented in the Appendix and in Table 3. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and

corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

(2) Approximately 9 percent of the tetrachloroethylene exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 30.6-fold. The remaining 91 percent of tetrachloroethylene exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of tetrachloroethylene, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding tetrachloroethylene concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding tetrachloroethylene concentrations. Because data indicating other sources of tetrachloroethylene exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the incremental risks associated with the indicated routes only.

Thus, the criterion associated with human lifetime carcinogenic risk of 10^{-5} is 8.0 ug/l. Because additional data are expected to be published in the near future, this criterion will be reevaluated at that time.

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APPENDIX

Derivation of Criteria for Tetrachloroethylene

Tetrachloroethylene administered by gavage to mice caused hepatocellular carcinomas in both males and females in the NCI bioassay at both the high and low dose levels. The males were treated at 1,072 and 586 mg/kg five times per week for 78 weeks and held until 90 weeks for observation. The observed incidences of hepatocellular carcinomas in these dose groups and the matched vehicle controls are shown in the table below.

The multistage model did not fit these data for tetrachloroethylene sufficiently well. Therefore, the high dose group was deleted and the criterion was recalculated. See the Human Health Methodology Appendices to the October 1980 Federal Register notice which announced the availability of this document for a complete discussion. With a fish bioaccumulation factor of 30.6 the parameters of the extrapolation model are:

Dose (mg/kg/day)	Incidence (No. responding/No. tested)
0	2/20
536 x 5/7 = 383	32/49
1,072 x 5/7 = 766	27/48*
le = 78 weeks	w = 0.026 kg
Le = 90 weeks	R = 30.6 l/kg
L = 90 weeks	

With these parameters the carcinogenic potency factor for humans, q_1^*, is 3.9776×10^{-2} $(mg/kg/day)^{-1}$. The result is that the water concentration should be less than 8.0 mg/l in order to keep the individual lifetime risk below 10^{-5}.

*Data was not used in the calculation of the criterion.